VA RESEARCH & DEVELOPMENT

Date: March 6, 2003
From: Chief Research & Development Officer (12)
Subj: Research and Development Stand Down
To: ACOS/R (151)

1. **Background:** In the eight short weeks since I assumed responsibility as Chief Research and Development Officer (CRADO), I have had to address a number of incidents concerning the protection of human subjects involved in interventional research studies that have the potential to put research subjects at risk. Those incidents include the falsification of individual patient data that contributed to the death of one or more patients; the inadvertent overdosing with a study medication of a research participant; an experimental procedure that was conducted without the prior approval of either the Institutional Review Board (IRB) or Research and Development (R&D) Committee; and a phase 4 drug study that was conducted without a principal investigator (PI) of record with clinical privileges to prescribe and monitor the study medication and the failure of an IRB to meet even the minimal standards required by the Common Rule.

2. While it is my belief that those incidents are exceptions to what is otherwise an outstanding human subjects research program, those practices will not be tolerated. I am, therefore, instituting a 90-day national VA human subjects research **stand down** effective Monday, March 10 through Friday, June 6, 2003. For the purposes of this activity, a stand down will **NOT** mean that research activities will cease, but rather, the purpose of this stand down is to focus attention on proactively reviewing the human study program to ensure we are doing all that is possible to ensure the protection of human subjects and the ethical conduct of research.

3. In the military, a "stand down" usually has two components: 1) shutting down all affected operations, and 2) focusing all activities on a) identification and correction of the problem, and b) education and training. While I could stop all human subjects research, I have not taken that course of action. In the military, a standing down of activities is done for two reasons. First, stopping the activity of concern (grounding all planes, for example) ensures that no further problems (such as crashes) occur during the stand down. Second, it allows those involved to focus the majority, if not all, of their time on identifying the cause of and correcting the problems for which the stand down was implemented.

4. However, in the current situation, neither of those likely would occur.
First, although we have dealt with a number of concerns during the past couple of months, those events are rare, and the chance that we would prevent others from now occurring is small. Second, doctors do much more with their time than research. Third, a stand down of research potentially could harm many of the patients who are dependent on the clinical interventions that we provide. Thus, this stand down will focus our efforts on identifying and correcting problems, as well as education and training.

5. **During this stand down the following will be achieved:**

a. Effective oversight of human studies research by an IRB and VA research committee will be verified.

Within 90 days, at any site conducting human studies research, the Medical Center Director, Chief of Staff, and Associate Chief of Staff for Research (ACOS/R) (or comparable person, if the hospital does not have an ACOS/R) will review the operations of the IRB and the R&D Committee and will attest, through the VISN Director to the Chief Network Officer and the Chief Research Officer to the fact that those committees are functioning at least at the minimum level required by the Common Rule and **M-3 Part I**,Chapters 2, 3, and 9. These requirements include that the IRB and R&D Committees are appropriately constituted and meet on a regular enough basis to provide timely review and oversight of new and continuing protocols and review of Adverse Events and Serious Adverse Events.

b. All individuals who are involved in human studies research will receive appropriate training in the ethical principles and accepted practices on which human studies research should be conducted.

All investigators, research coordinators and research assistants involved in human studies research and all members of the Research Office, all members of the R&D Committee, and all members and staff of a VA Institutional Review Board (IRB), exclusive of secretarial support, will complete an educational course or complete a web-based course on **both** the protection of human research subjects, as well as Good Clinical Practice (GCP). (If the University affiliate provides the VA IRB function, the affiliate will be encouraged to participate in these educational activities.) Investigators who can document completion of these courses in the past year will not be required to re-take the training at this time. All individuals subject to this policy will be required to update their training annually, thereafter. VA investigators should use the National Cancer Institute's web-based course on Human Participant Protections Education for Research Teams. Over the next two weeks ORD will

develop computer-based training in GCP. CD-ROMs will be provided to any site that does not have Internet access.

c. An effective credentialing process for all individuals involved in human studies research will be verified.

Any research personnel who perform independent clinical activities (judgment based independent of the research protocol) as part of their research activities will be allowed to conduct such activities only if they are credentialed and privileged to provide those activities on patients by the standard credentialing and privileging process of the facility (e.g., doctors, clinical psychologists). All such individuals whether compensated or on a WOC appointment will be credentialed through VetPro. All other individuals involved in human studies research (whether a licensed Title 38 individual, such as a nurse, or a Title 5 employee; and whether the individual receives VA compensation or is without compensation (WOC)) will have their credentials confirmed, a scope of work established and a record of such maintained and available for review. Licensed individuals will have their license(s) confirmed yearly. Facilities will create an electronic means of tracking all WOC employees involved in human subjects research to facilitate the regular checking of these individuals against exclusionary lists. Full instructions will be sent within 7 days of the start of this stand down.

d. Disciplinary actions that may result from noncompliance with the ethical standards of human study oversight.

6. All investigators involved in human studies research will be notified that that a) if they conduct research without IRB approval, it will affect their standing in the VA and b) PIs will be held responsible for ethical breaches in the conduct of their research and these problems may affect the PI's ability to do research with the VA in the future.
7. The steps outlined above will be further discussed on Monday's R&D Hotline. I am confident that these activities will enable us to identify and correct any problems in our human subjects research programs, help us to properly educate and train our researchers, and ensure the protection of our most valuable assets—the veterans who participate in our investigative trials.

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